November 23, 1951

Dr. Bernard D. Davis
Tbc Research Lab., USPHS
411 E. 69 Street
New York 21, N.Y.

Dear Bernie:

Thank you for the sample of washed agar (rec'd airmail!) and your letter of the 21st with its interesting information. Gunny and Roger wanted to look for Pseudomonas mutants requiring the Pyruvate Oxidation Factor, and I had sent them PF-11 as a previous unknown, so that your information (which I shall relay promptly) will be quite useful.

As to PF-21, I should be willing to accept your judgment on writing a note, and as to whether you should appear as sole or senior author. If you do think itbworthwhile (and the industrial application of the coli mutant points to the utility) to advertise it, I would suggest sending the note to Archives, and unless you want to assume the full burden of its distribution, also depositing the mutant with the ATCC (if they can be relied on for such things). The leucine requirement is revertible, and it might be worthwhile to get it out, both for simplification of the medium, and possibly to help if the leucine-requirement has something to do with the inhibitions. The mutant is derived from Stanier's A3.12 strain (J. Bact, 59:117-127 1950, 54:339-348 1947, and especially 55:477-94 1948). Following enrichment by the pehicillin method, the mutant was detected by means of replica plating.

My prompt response is directed mainly at your editorial. I think the biological approach to bacteria should be hammered home at every possible occasion. However, my own experience is that it takes a year to reach a proper philosophical understanding of Luria and Delbruck's analysis. This was the main reason (Harry Eagle was the second) for the note "Replica plating and indirect selection of bacterial mutants" by J. and E.M. Lederberg, which is due of the January 1952 issue of J. Bact. The success of indirect selection obviates the difficulty you pose on p. 4, lines 6-10. I would not go so far as to suggest you modify your editorial at this late date, but I would not be unhappy to have indirect selection interpreted to your Masses at this or any other occasion. (By the way, I think your leg is being pulled over the footnote p.5, unless you mean "interpretation of the experimental results". See p. 493-494 of their paper.) I enclose an essentially final draft of the ms. Back to the editorial, why don't you use this occasion to clear up Graessle & Pietrewski's paper on the interaction of sm e (J. Bact. 57:459)?

Whilewwe're discussing antibioties, I'd like to tell you about something that's either infuriating or amusing, according to how you look at it. You know the paper by Smith, Oginsky, and Umbreit, in the series on sm action mechanism, dealing with metabolism of S^r strains (J. Bact.58?961). Roger was particularly impressed by the statement that S^r strains are not improved in growth by aeration. This was not in accord with my own experience, so after verifying that our S^r were not distinguishable by this test from S^s, I wrote the Merck people asking for their cultures for verification. Some time later, I received their "Murray" strains, s and r, with a note stating that the published metabolic differences had been checkedbut not the aeration effect: they were busy with other problems. In my hands, the s and r strains were no different, and I wrote back accordingly. I was astonished to receive a reply that they were not surprised at this, for they had run into the same thing many times since their original experiments. (In my first letter I had specifically asked for strains to verify the aeration effect). They claim, however, that after continued cultivation for six mos. some of the strains did give rise to the non-aerobic type-- would I be interested to try that! They admit that they "do not know whether it is a matter of chance that the organism loses the ability to respond to air". If I could have found all of this out in the first place, it would not be so disturbing. Not to change the subject very drastically, I was pleased to see Clough's note in PNAS, but do wish he could have been more concise.

Stanier had a good idea about this (because he believed what he read), which unfortunately won't work: that the non-aerobic type is similar to the petite yeast of Ephrussi's, and results from the direct action of sm on the oxidation system. The spontaneous S^r mutants are able to survive selection with S^r, but are stripped of the system. In K-12 this could have been tested genetically; otherwise, S^r obtained by indirect selection would have given a very appropriate test-- too bad. Anyhow, it might still be a good idea to look out for analogous forms.

Sincerely,

Joshua Lederberg

P.S. Methionine-less has occurred at least six times as a one-step auxotroph. Haven't you ever hit it? Perhaps it occurs less often in W. It has also come up in Salmonella.

in coli